## AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings of claims in the application:

## LISTING OF CLAIMS:

- 1. (original) A transgenic non-human animal expressing at least one transgene comprising a DNA sequence encoding a heterologous Amyloid Precursor Protein(APP) comprising at least the Arctic mutation (E693G) and a further AD (Alzheimer's disease) pathogenic mutation or a further transgene affecting AD pathogenesis, which results in increased amounts of intracellular soluble A $\beta$  aggregates, including A $\beta$  peptides.
- 2.(original) The transgenic animal according to claim 1, wherein the transgene/transgenes are integrated in the genomic DNA.
- 3.(currently amended) The transgenic animal according to claim 1 [[or 2]], wherein said transgene/transgenes are operably linked to a promoter effective for expression of said gene in the brain tissue of said animal.
- 4.(currently amended) The transgenic animal according to any of claims  $1\ 3$  claim 1, wherein the endogenous APP is expressive or non-expressive.
- 5.(currently amended) The transgenic animal according to any of claims 1-4 claim 1, wherein said further transgene is a human presentilin-1 and/or presentilin-2 transgene harboring an AD pathogenic mutation.
- 6. (currently amended) The transgenic animal according to any of claims 1-4 claim 1, wherein said further transgene comprises a DNA sequence encoding apolipoprotein E, apolipoprotein J(clusterin),  $a_1$ -antichymotrypsin (ACT) or fragments thereof.
- 7. (currently amended) The transgenic animal according to any of claims 1-4 claim 1, wherein said further AD pathogenic mutation is one of the APP mutations KM670/671DF, KM670/671DY, KM670/671EF or KM670/671EY.
- 8.(currently amended) The transgenic animal according to any of claims  $1\ 4$  claim 1, wherein said further AD pathogenic mutation is one of the APP

mutations KM670/671NL, KM670/671NY, KM670/671NF, KM670/671KL, KM670/671DL or KM670/671EL, wherein KM670/671NL (the Swedish mutation) is preferred.

- 9.(currently amended) The transgenic animal according to any of claims 1-4 claim 1, wherein the transgenic animal expresses only one transgene which comprises only the Arctic mutation (E693G) and the Swedish mutation (KM670/671NL).
- 10.(currently amended) The transgenic animal according to any of claims 1.9 claim 1, additionally comprising a homologously integrated targeting construct for at least one of the neprilysin or insulin-degrading enzyme (IDE) genes, which disrupts these genes through gene ablation (knock-out) and enhances A $\beta$ -40 and/or A $\beta$ -42 Arctic peptide production.
- 11.(currently amended) The transgenic animal according to any of claims 1  $\frac{10}{10}$  claim 1, wherein the transgenic animal is a rodent.
- 12.(currently amended) The transgenic animal according to any of claims 1-11  $claim\ 1$ , wherein the transgenic animal is a murine animal.
- 13.(currently amended) The transgenic animal according to  $\frac{\text{claim 1 12}}{\text{claim 1}}$  wherein the transgenic animal is a mouse.
- 14.(currently amended) A method of producing the transgenic animal according to any of claims 1 13 claim 1, comprising integrating in the genomic DNA at least one transgene comprising a DNA sequence encoding a heterologous Amyloid Precursor Protein (APP) comprising at least the Arctic mutation (E693G) and a further AD (Alzheimer's disease) pathogenic mutation or a further transgene affecting AD pathogenesis.
- 15.(original) The method according to claim 14, wherein said transgene/transgenes are operably linked to a promoter effective for expression of said gene in the brain tissue of said animal.
- 16.(currently amended) The method according to any of claims 14 15 claim 14, wherein the endogenous APP is optionally made non-expressive.
- 17.(currently amended) The method according to any of claims 14-16 claim 14, wherein said further transgene is a human presentiin-1 and/or presentiin-2 transgene harboring an AD pathogenic mutation.

- 18.(currently amended) The method according to any of claims 14-16 claim 14, wherein said further transgene comprises a DNA sequence encoding apolipoprotein E, apolipoprotein J (clusterin), al-antichymotrypsin (ACT) or fragments thereof.
- 19.(currently amended) The method according to any of claims 14 claim 14, wherein said further AD pathogenic mutation is one of the APP mutations KM670/671DF, KM670/671DY, KM670/671EF or KM670/671EY.
- 20.(currently amended) The method according to any of claims claim 14, wherein said further AD pathogenic mutation is one of the APP mutations KM670/671NL, KM670/671NY, KM670/671NF, KM670/671KL, KM670/671DL or KM670/671EL, wherein KM670/671NL (the Swedish mutation) is preferred.
- 21.(currently amended) The method according to any of claims 14 20 claim 14, additionally comprising homologously integrating a targeting construct for at least one of the neprilysin or insulin-degrading enzyme (IDE) genes.
- 22.(currently amended) A method of screening, wherein the transgenic animal according to any of claims  $1 \cdot 13$  claim 1 is used for screening for agents useful for treating, preventing or inhibiting Alzheimer's disease.
- 23.(currently amended) A method of screening, wherein the transgenic animal according to any of claims 1-13 claim 1 is used for screening for diagnostic agents for Alzheimer's disease.